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# PRE-APPEAL BRIEF REQUEST FOR REVIEW

Docket Number (Optional): 1385.45510VX1

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to "Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450" [37 CFR 1.8(a)]

on _____

Signature _____

Typed or printed name _____

| Application Number | Filed |
|---|---|
| 10/087,942 | March 5, 2002 |

First Named Inventor: Robert L. CAMPBELL

| Art Unit | Examiner |
|---|---|
| 1631 | BRUSCA, John B. |

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

I am the

☐ applicant/inventor.

☐ assignee of record of the entire interest.
See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed.
(Form PTO/SB/96)

☒ attorney or agent of record.
Registration number 39,397.

☐ attorney or agent acting under 37 CFR 1.34.
Registration number if acting under 37 CFR 1.34 _____

Signature

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June 13, 2006
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required.
Submit multiple forms if more than one signature is required, see below*.

☐ *Total of _____ forms are submitted.

## ARGUMENTS FOR REQUEST FOR PRE-APPEAL CONFERENCE

I. Claim 30 Complies With The Enablement Requirements Of 35 U.S.C. §112, First Paragraph

The Office Action indicates that the specification did not provide specific guidance for practicing the invention, and that there are no paragraph numbers in the specification as filed.

Applicants never directed reference to the specification as filed. Applicants indicated that:

> As discussed in the specification, these compounds can include peptides, proteins, carbohydrates, nucleic acids, and lipids (e.g., free fatty acids, triglycerols, steroids). See paragraphs [0022], [0063], and [0150] of the published application. (Emphasis added).

See page 21, lines 16-19 of Applicants' Amendment dated October 28, 2005. It was clearly not Applicants' intention to refer to the specification as filed. The paragraphs of the published application correspond to page 6, lines 5-22; page 17, lines 6-19; and page 44, line 27 to page 45 line 2 of the specification as filed.

The claimed invention satisfies the requirements of *In re Wands*. 8 USPQ2d 1400 (Fed. Cir. 1988). Applicants note that the nature of the art is such that one must necessarily perform assays to determine the effect of different peptides and/or medium components on the production of antibiotics, steroids, carbohydrates, lipids, and nucleic acids in cultured cells. A conventional experiment, for example, may necessitate assaying of a large number culture media, while the present invention would require assaying of a reduced number of culture media that accurately represents all possible culture media. With respect to factor 2, the specification need only enable practice of the invention.

Regarding factor #3, as previously discussed, there is no requirement for providing a tutorial. The specification need only be sufficient to enable one skilled in the art to understand and practice the invention. The present invention provides an ability to significantly reduce the actual number of screenings performed while increasing the size of the culture media libraries

considered, resulting in a reduction of the amount of screening necessary. Regarding factors 5-7, the skill of those in the art of cell culture assays is high, and a skilled artisan is would readily appreciate the advantages (e.g., costs and time) associated with a reduction in the number of assays performed while increasing the size of the library that can be considered.

II. Claim 128, and claims 2-10, 13-15, and 18-28 depending therefrom are patentable

The Office Action does not make a *prima facie* case of obviousness predicated on the teachings of Lam, Zheng, Bause, and the Invitrogen catalog. First, there is no suggestion or motivation in Lam to modify, combine, or seek out the teachings of three (3) additional references. Second, there is no realistic expectation of success from combining the four (4) references. Finally, the combination of references still fails to clearly teach or suggest all the limitations recited in claim 128.

Regarding the first factor, the Office Action also does not provide any credible indication as to where motivation exists, in Lam, to seek out the teachings of the teachings of the remaining three references for purposes of arriving at the claimed invention. Three of the references (namely Lam, Zheng, and Bause) appear to be in different fields of endeavor. Lam relates to peptide screening for identification and characterization of ligands. Zheng relates to medicinal chemistry and targeted combinatorial libraries. Additionally, Zheng's methodology is directed to the discovery of compounds in-vivo. Bause relates to the study of structural requirements of N-glycosylation of proteins as conformational probes. In contrast, the present invention relates to identification of medium components for pharmaceutical design, drug discovery, and identification and/or design of peptides with particular pharmacological or therapeutic activities.

The Office Action does not indicate why a skilled artisan working to identify and characterize ligands (as Lam discloses) would seek out the teachings of Zheng, which relate to targeted combinatorial libraries, for purposes of modifying their system. It is an even further

stretch for a skilled artisan to additionally seek out the teachings of Bause, which relate to proline peptides as conformational probes. Even if the teachings of Zheng and Bause were sought, it is not clear how, or why, one working to identify and characterize ligands would suddenly derive a method for identifying medium components by reading these three references without the benefit of hindsight.

Regarding the second factor, three of the four references are in different fields of endeavor. The Office Action does not indicate why, or how, there could be a realistic expectation of success from combining these three references.

Regarding the third factor, even if the references were properly combinable, they would still fail to disclose or suggest all the features recited in claim 128. The Office Action admits that Lam fails to disclose features of the claimed invention such as: (1) the RPMI medium being a synthetic medium, (2) utilization of a space-filling analysis to measure properties, (3) determination of parameters of the first library before screening, or (4) determination of functions of quantitative structure activity relationships (QSAR) analysis. The Office Action relies on the Invitrogen catalog for showing that the RPMI medium consists entirely of defined compounds, and on Zheng for disclosing a method of constructing and refining a peptide library by use of QSAR analysis. Bause is relied upon for disclosing the analysis of peptide sequences by consideration of space-filling parameters.

Lam, however, also fails to provide any disclosure or suggestion for additional features recited in independent claim 128. Lam provides assays for biological activity of a bio-oligomer from a library treated for removing any toxic molecules remaining from synthesis. Lam assays random peptide libraries on beads added to cells in growth media. Lam never identifies a predetermined set of test compounds. Further, because Lam assays random peptide beads, it is not possible to clearly determine the effect of individual and/or predetermined compounds (or individual peptides).

Lam further fails to construct a first test library as set forth in the claimed invention. Lam discusses preparation of beads that are selectively cleavable from the solid-phase support. This differs from the claimed identification of a predetermined set of test compounds. Lam does not parameterize predetermined test compounds by determining a specific parameter for each test compound. Since Lam fails to perform a space-filling design (as admitted in the Office Action), then Lam must necessarily fail to provide a library of first culture media that contain at least one first test compound identified by the space-filling design.

Lam does not apply a quantitative relationship to estimate the indicia of candidate test compounds that are not in the first test library (i.e., ligands that were not screened during the first round, or beads that were not in the library). Lam also does not select a second test library containing candidate test compounds that were not in the first test library.

The 'second library' disclosed by Lam is "based on the common sequences of the ligands selected during the first screening." See col. 17, lines 19-24. Lam appears to identify higher levels of activity by merely setting a more stringent threshold level for re-screening selected ligands identified in the first library.

The Office Action next alleges that Zheng discloses a method of constructing and refining a peptide library by use of QSAR analysis, and constructing libraries that are most likely to have a desired activity. Zheng discloses a method for rational design of targeted combinatorial libraries. The method seeks to select a subset of available building blocks that are most likely to be present in active compounds. For example, Zheng describes the design of a targeted library with bradykinin (BK) potentiating activity. The methodology begins with twenty eight (28) known BK potentiating pentapeptides that are used as a training set. Thus, the initial peptides are known to provide certain levels of activity. By using these initial 28 BK potentiating peptides as a training set, the representative space does not encompass the entire pentapeptide space. Further, the peptide are biased toward certain activity. Consequently, any

peptides that are subsequently identified will necessarily be close in space to the 28 initial peptides, and also display similar activities.

Nonetheless, Zheng still fails to perform various steps recited in the claimed invention. For example, Zheng never identifies a predetermined set of compounds and never performs a space-filling design to identify first test compounds that are a subset of the predetermined set of compounds and also representative of the entire space occupied by the predetermined set of test compounds. Rather, Zheng's methodology begins with peptides known to have desired levels BK potentiating activity.

The Office Action also indicates that Bause discloses the analysis of peptide sequences by consideration of space-filling parameters. While Bause discusses a space-filling model of a particular hexapeptide, such a model does not appear to correspond to a space-filling design that is intended to represent, for example, a peptide/compound space. Rather, it appears to be a three-dimensional structure of the peptide which identifies potential sugar-attachment sites. However, Bause still fails to provide any disclosure or suggestions for the aforementioned features recited in independent claim 128 and not disclosed by the remaining references.

The combination of references simply fails to suggest features of the claimed invention, such as:

> determining a quantitative relationship between the measured indicia of the property, and at least one parameter of the plurality of first test compounds;
>
> calculating an estimated indicia for a plurality of candidate culture media using the determined quantitative relationship, wherein each candidate culture medium contains a respective candidate test compound from the predetermined set of test compounds that is not in the first test library;
>
> setting a test requirement having a test indicia range;
>
> selecting a second test library comprising at least one second culture medium, wherein each second culture medium is a candidate culture medium having an estimated indicia that satisfies the test requirement;
>
> measuring the indicia of the property of the at least one second culture medium; and
>
> identifying at least one second culture medium having a measured indicia that satisfies the test requirement.

For all the foregoing reasons, the pending rejections should be withdrawn.